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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/051,412	01/17/2002	Uwe Joerg Ries	5/1313	9079

28505 7590 08/25/2003

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EXAMINER	
ANDERSON, REBECCA L	
ART UNIT	PAPER NUMBER
1626	

DATE MAILED: 08/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/051,412	RIES ET AL.	
	Examiner	Art Unit	
	Rebecca L Anderson	1626	

-- The MAILING DATE of this communication appears on th cov r sheet with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8* is/are pending in the application.

4a) Of the above claim(s) *4 and 8* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3 and 5-7* is/are rejected.

7)☒ Claim(s) *1-3 and 5-7* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2 total* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Claims 1-8 are currently pending in the instant application. Claims 1-3 and 5-7 are rejected, claims 1-3 and 5-7 are objected and claims 4 and 8 are withdrawn from further consideration as being drawn to non-elected inventions.

Election/Restrictions

Applicant's election of Group I, claims 1-7 and the species of compound 4, 2-(3-carbamimidoyl-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-isobutyramide in the paper mailed 02 July 2003 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

The election of compound 4, 2-(3-carbamimidoyl-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-isobutyramide has resulted in the following generic concept: The product of the formula (I) wherein:

R1 denotes pyrrolidinocarbonyl

R2 denotes a hydrogen atom or an (unsubstituted) C1-3 alkyl group,

R3 denotes a hydrogen atom or a C1-3-alkyl group,

R4 denotes denotes a hydrogen atom or an (unsubstituted) C1-3-alkyl group,

Ar denotes a phenyl group substituted by the groups R5, R6 and R7,

R5 denotes an (unsubstituted) amidino group,

R6 denotes a hydrogen atom or a C1-3-alkyl group,

R7 denotes a hydrogen atom or a C1-3-alkyl group,

R8 denotes a hydrogen atom or an (unsubstituted) C1-3-alkyl group and

R9 denotes a hydrogen atom or an (unsubstituted) C1-3-alkyl group.

The remaining subject matter of claims 1-3 and 5-7 that is not drawn to the elected invention identified supra and claims 4 and 8 stand withdrawn from consideration as being drawn to a non-elected invention, 37 CFR 1.142 (b).

The remaining compounds which are not within the generic concept, which are independent and distinct from the generic concept and do not have unity with the species elected and therefore are withdrawn by means of a restriction requirement within the claim are, for example, the compounds wherein:

R1 denotes a C3-7 –cycloalkyl-carbonyl group, a phenylcarbonyl, naphthylcarbonyl or heteroarylcarbonyl group, a C1-3-alkyl group monosubstituted by a hydroxy group or terminally disubstituted by a phenyl and a hydroxy group, a 4-7 membered cycloalkyleneimino-carbonyl (except pyrrolidinocarbonyl)l or cycloalkyleneimino-sulphonyl group, a C3-7-cycloalkylamino group,

R2 denotes a fluorine, chlorine or bromine atom or a C1-3-alkyl group wherein the hydrogen atoms are wholly or partly replaced by fluorine atoms, a hydroxy or C1-3-alkoxy,

R4 denotes a C1-3-alkyl group substituted by a carboxy group or a group which may be converted into a carboxy group in vivo,

Ar denotes a phenyl substituted by the groups R5, R6 and R7 wherein

R5 denotes a cyano group, an amidino group substituted by one or two C1-3-alkyl groups, an amino-C1-3-alkyl, C1-3-alkylamino-C1-3-alkyl or di-(C1-3-alkyl)amino-C1-3-alkyl group,

R6 denotes a fluorine, chlorine or bromine atom, a trifluoromethyl, hydroxy, hydroxy-C1-3-alkyl, C1-3-alkoxy, C1-3-alkoxy-C1-3-alkyl, carboxy, carboxy-C1-3-alkyl, carboxy-C1-3-alkoxy, C1-4-alkoxy-carbonyl-C1-3-alkoxy, phenyl-C1-3-alkoxy, amino, C1-3-alkylamino or di-(C1-3-alkyl)amino group

R7 denotes a fluorine, chlorine or bromine atom

Naphthyl substituted by the groups R5, R6, R7, or a thienylene, thiazolylene, pyridinylene, pyrimidinylene, pyrazinylene or pyridazinylene group

R8 and R9 each denote a C1-3-alkyl group substituted by a phenyl or heteraryl group or an amino group.

Some specific species of the withdrawn compounds are the species of examples

(7) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(piperidin-3-yl-carbonyl)-phenyl]-acetamide,

(8) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-(3-methyl-4-benzoyl-phenyl)-acetamide,

(9) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-methyl-4-(1-hydroxy-1-phenyl-methyl)-phenyl]-acetamide,

(10) 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-{4-[1-(3-carbamimidoyl-phenyl)-1-hydroxy-methyl]-3-methyl-phenyl}-acetamide,

(11) 2-(3-carbamidoyl-phenyl)-N-[3-methyl-4-(pyridin-3-yl-carbonyl)-phenyl]-isobutyramide,

, etc.

The above mentioned withdrawn compounds which are withdrawn from consideration as being for non elected subject matter differ materially in structure and

composition from the compounds of the elected invention. The withdrawn compounds contain varying functional groups which differ from those of the elected invention such as thienyl, thiazolyl, pyrimidinyl, pyrazinyl, pyridazinyl, etc. which are chemically recognized to differ in structure and function. This recognized chemical diversity of the functional groups can be seen by the various classification of these functional groups in the U.S. classification system, i.e. class 549 subclass 29(+) (thienyl), class 548 subclass 146(+) (thiazolyl), class 544 subclass 242(+) (pyrimidinyl), class 544 subclass 336(+) (pyrazinyl), class 544 subclass (224(+) (pyridazinyl), etc. Therefore, again, the compounds which are withdrawn from consideration as being for non elected subject matter differ materially in structure and composition and have been restricted properly as a reference which anticipated but the elected subject matter would not even render obvious the non-elected subject matter.

These withdrawn compounds are independent and distinct from the elected invention and do not have unity with the species elected and are therefore withdrawn by means of a restriction requirement within the claims.

Applicants' claims involve more than one independent or distinct invention. Under 35 U.S.C. 121, the claims may be restricted and the examination limited to a restricted invention.

The withdrawn subject matter of claims 1-8 is properly restricted as it differs materially in structure and element from the elected subject matter identified supra so as to be patentably distinct there from. A reference, which anticipated but the elected

subject matter would not even render obvious the non-elected subject matter.

Accordingly, restriction, as has been required is proper.

Claim Objections

Claims 1-3 and 5-7 are objected to as containing non-elected subject matter.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3, 6 and 7 are rejected under 35 USC 12 2nd paragraph for failing to particularly point out and distinctly claim the subject matter which the applicant regards as his invention. Specifically, a broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claims 1-3 recite the broad recitation of the carboxylic acid amide of the formula (I) and the claims also recite

specific compound names which are the narrower statement of the range/limitation. For example, claim 1 recites the carboxylic acid amide of the formula (I) and also recites the compound 2-(5-carbamimidoyl-2-hydroxy-phenyl)-N-[3-chloro-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-acetamide which is a narrower statement of the generic formula (I), specifically, the specific compound mentioned above, R1 denotes a 4 to 7 membered cycloalkyleneimino-carbonyl group, R2 denotes a chlorine atom, R3 denotes a hydrogen, R4 denotes a hydrogen, R8 denotes a hydrogen, R9 denotes a hydrogen and Ar denotes a phenyl substituted by R5, R6 and R7 wherein R5 denotes an amidino group, R6 denotes a hydroxy group and R7 denotes a hydrogen group. This rejection can be overcome by deleting the specifically named compounds from claims 1-3. The applicant could also add new claims drawn solely to the specifically named compounds from claims 1-3 that fall within the elected invention identified supra.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 1-3 and 5-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 00/71512.

Applicant's instant elected invention of claims 1-7 teach the compound of formula (I) wherein:

R1 denotes pyrrolidinocarbonyl,

R2 denotes a hydrogen atom or an (unsubstituted) C1-3 alkyl group,

R3 denotes a hydrogen atom or a C1-3-alkyl group,

R4 denotes denotes a hydrogen atom or an (unsubstituted) C1-3-alkyl group,

Ar denotes a phenyl group substituted by the groups R5, R6 and R7,

R5 denotes an (unsubstituted) amidino group,

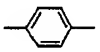
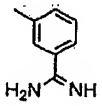
R6 denotes a hydrogen atom or a C1-3-alkyl group,

R7 denotes a hydrogen atom or a C1-3-alkyl group,

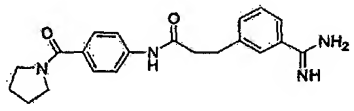
R8 denotes a hydrogen atom or an (unsubstituted) C1-3-alkyl group and

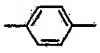
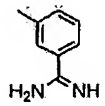
R9 denotes a hydrogen atom or an (unsubstituted) C1-3-alkyl group. (claim 1, 2) and wherein: R1 is in the 4 position of the phenyl group, R5 is in the 3 position if R6 denotes a hydrogen atom or position 5 if R6 is other than hydrogen (claim 3). Claim 5 teaches specific compounds such as 2-(3-carbamimidoyl-phenyl)-N-[3-methyl-4-(pyrrolidin-1-yl-carbonyl)-phenyl]-isobutyramide. Claim 6 teaches a physiologically acceptable salt of the compound of formula (I) and claim 7 teaches a pharmaceutical composition of the compound of formula (I).

Determining the scope and contents of the prior art

The prior art WO 00/71512 discloses compounds of the formula A-Y-D-E-G-J-Z-L (pages 4) which are useful for the treatment of disease states (page 10) characterized by undesired thrombosis. Page 16 of the prior art discloses a preferred embodiment for the compound of formula A-Y-D-E-G-J-Z-L wherein G can be –CR7R8. A further preferred embodiment of the compound of formula A-Y-D-E-G-J-Z-L is found on page 31 wherein A can be  , Y can be –C(=O)-, D can be  , E can be –N(H)-C(=O)-, J is a direct link (page 32), and Z-L can be  . Page 94 of the prior art reference discloses the compound of example 24:

Example 24. Preparation of N-[4-(1-pyrrolidinylcarbonyl)phenyl]-3-(3-amidinophenyl)-propionamide.



which has a value for A corresponding to  , a value for Y corresponding to –C(=O)-, a value for D corresponding to  , a value for E as –N(H)-C(=O)-, a value for J corresponding to a direct link and a value for Z-L corresponding to  . This species example disclose further preferences towards these specific values. Pages14 and 15 of the prior art discloses pharmaceutically acceptable salts of the compounds of the formula A-Y-D-E-G-J-Z-L such as acid addition salts and base addition salts. Pages 53 and 54 disclose pharmaceutical compositions comprising the compound of the formula A-Y-D-E-G-J-Z-L and provides specific acceptable carriers, excipients and stabilizers and a preferred dosage.

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the instant elected invention is that the prior art does not disclose a specific species example which falls within applicants instant elected invention. The prior arts example 24 differs from the instantly elected invention in the value for G, but there are other preferred embodiments of the prior art invention which have the value for G as –CR7R8 as discussed above. Furthermore, the

preferred embodiment of G as discussed above provides for only two possible substituents for the value of G, which provide motivation to prepare compounds with both of the possible substituents. Also, the prior art does generically disclose the compound of A-Y-D-E-G-J-Z-L which encompasses applicants instant invention and provides ample direction and guidance in the form of preferred embodiments as to the preferred substituents for A, Y, D, E, G, J, Z and L.

Resolving the level of ordinary skill in the pertinent art and considering objective evidence present in the application indicating obviousness or nonobviousness

Minus a showing of unobvious results, it would have been obvious to one of ordinary skill in the art at the time of the invention to create compounds which fall within applicants elected invention in order to prepare more compounds as found in the prior art of WO 00/71512 for antithrombotic treatment. The motivation is found in the prior art of WO 00/71512 which provides ample direction and guidance in the form of preferred embodiments and specific examples, and therefore, provides the motivation to prepare the compounds of applicants instant elected invention since these are the preferred compounds of WO 00/71512. The motivation is to prepare more compounds which are usefule for antithrombotic treatment.

Conclusion

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (703) 605-1157. Mrs. Anderson can normally be reached Monday through Friday 7:00AM to 3:30PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph McKane, can be reached at (703) 308-4537.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone numbers are (703) 308-1235 and (703) 308-0196.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45AM to 4:45PM. The telecopier numbers for accessing the facsimile machine are (703) 308-4242, (703) 305-3592, and (703) 305-3014.

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